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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,978	11/19/2004	Patrick Hwu	230591	4494

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EXAMINER	
DUFFY, BRADLEY	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/508,978	HWU ET AL.	
	Examiner	Art Unit	
	BRADLEY DUFFY	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,8,11-22,25,28-30,58-63 and 68* is/are pending in the application.

4a) Of the above claim(s) *1-5,8,11-22,25,28-30,58,60-63 and 68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/14/08, 4/30/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 14, 2008, has been entered.

1. The amendment filed on February 14, 2008, is acknowledged and has been entered. Claims 66 and 67 have been canceled. Claim 68 has been newly added.

2. Claims 1-5, 8, 11-22, 25, 28-30, 58-63 and 68 are pending in the application. Claims 1-5, 8, 11-22, 25, 28-30, 58, 60-63 and 68 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in the reply filed January 18, 2007.

3. Claim 59 is under examination.

4. The following Office action contains NEW GROUNDS of rejection.

Election/Restriction

5. The amendment filed February 14, 2008 presents new claim 68, which is directed to an invention that lacks unity with the originally elected invention for the following reasons:

In this case, the method of claim 68 does not relate to the same single general inventive concept under PCT Rule 13.1 as the method of originally elected claim 59, because, under PCT Rule 13.2, they lack the same or corresponding special technical feature.

For the reasons set forth in the restriction requirement mailed 9/16/2206, the special technical feature of the elected invention is inducing apoptosis of a natural killer (NK) cell comprising contacting the NK cell with an IL-21 polynucleotide encoding an IL-21 polypeptide, such as a polypeptide comprising the amino acid sequence of SEQ ID NO: 6 or 8, in an amount effective to induce apoptosis of the NK cell.

However, the special technical feature of newly presented claim 68 is decreasing the number of natural killer (NK) cells in a host, comprising administering to a host a polynucleotide encoding SEQ ID NO: 6 or 8 in an amount effective to decrease the number of NK cells in the host.

Therefore, it is apparent that newly presented claim 68 is drawn to a method that has a different special technical feature than the special technical feature of the elected invention because claim 68 recites the method objective of decreasing the number of natural killer cells in a host, while the originally elected invention recites the method objective of inducing apoptosis in a natural killer cell. Since the number of natural killer cells in a host depends on multiple dynamic processes such as NK cell proliferation and NK cell death, it cannot be known what effect inducing apoptosis of natural killer cells may or may not have on the number of natural killer cells in a host because other processes also affect NK cell number *in vivo*. Therefore, it is submitted that each of these different methods would require the correlation of a different endpoint and for these reasons do not relate to the same single general inventive concept under PCT Rule 13.1. Furthermore, it is noted that PCT Rules 13.1 and 13.2 do not provide for a single general inventive concept to comprise more than the first mentioned product, the first mentioned method for making said product, and the first mentioned method for using said product. Accordingly, this newly presented

method for using a polynucleotide encoding SEQ ID NO: 6 or 8 does not form a single general inventive concept with the original elected method.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 68 is withdrawn from consideration as being directed to a nonelected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Applicant is further reminded that applicant cannot, as a matter of right, file a request for continued examination (RCE) to obtain continued examination on the basis of claims which the examiner holds are drawn to an invention other than the one elected (see MPEP § 819 and 821.03).

Information Disclosure Statement

6. The references cited in the information disclosure statements filed on February 14, 2008, and April 30, 2008, have been considered.

Priority

7. With respect to the issue of priority, Applicant has not submitted any evidence or arguments in the reply filed February 14, 2008, that claim 59 should receive benefit under USC §§ 119 and/or 120 of the earlier filing date of the 60/368,438, filed March 27, 2002.

Claim 59 does not properly benefit under 35 U.S.C. § 120 by the earlier filing dates of the priority document claimed, since the claim is rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description and/or a sufficiently enabling disclosure.

Again, to receive benefit of the earlier filing date under 35 USC §§ 119 and/or 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the

invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Accordingly, the effective filing date of claim 59 is deemed the filing date of PCT/US03/09707, namely March 23, 2003.

Grounds of Objection and Rejection Withdrawn

8. Unless specifically reiterated below, the grounds of objection and rejection set forth in the previous Office action mailed October 18, 2007, have been obviated or rendered moot by Applicant's amendment and/or arguments filed February 14, 2008 or are moot in view of the NEW GROUNDS of rejection detailed below.

Response to the Declaration under 37 C.F.R. § 1.132

9. While the merit of the declaration under 37 C.F.R. § 1.132 filed February 14, 2008, and Applicant's arguments with respect to the rejection of the claim 59 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement as set forth in the last Office action have been considered, this declaration and these arguments are moot in view of the NEW GROUNDS of rejection of claim 59 under 35 U.S.C. 101 and under 35 U.S.C. 112, first paragraph, detailed below.

Response to the Statement under 37 C.F.R. 1.57 (f)

10. The statement under 37 C.F.R. 1.57 (f) filed February 14, 2007 is insufficient to satisfy the requirements set forth in 37 C.F.R. 1.57 (f) because the statement merely states that the material being inserted ***represents*** material

incorporated by reference, rather than stating that the material being inserted ***is*** the material incorporated by reference, as required by 37 C.F.R. 1.57 (f). Is the material being inserted **the same** as the material incorporated by reference or not? For the reason, the Examiner submits that a new statement *under 37 C.F.R. 1.57 (f)* executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted ***is*** the material previously incorporated by reference and that the amendment contains no new matter is required.

Grounds of Objection Maintained

Response to the Amendment

11. The objection to the amendment filed August 8, 2007, under 35 U.S.C. 132(a) because it introduces new matter into the disclosure[1], is maintained. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the addition of the sequences of SEQ ID NOs: 6, 7, 8, and 9 to the specification.

At page 10 of the amendment filed February 14, 2008, Applicant has remarked that the objection should be withdrawn because "the requirements for a proper incorporation by reference have been met".

However, while it appears that the Applicant made a *bona fide* attempt to comply with the requirements set forth in 37 C.F.R. 1.57 (f), the Examiner submits that the requirements for a proper incorporation by reference have not been met, because, as set forth in the above response to the Statement under 37 C.F.R. 1.57 (f), the statement merely states that the material being inserted ***represents*** material incorporated by reference.

[1] This objection also applies to the amendment to the specification filed 2/14/2008 which similarly introduces SEQ ID NOs: 6, 7, 8, and 9 into paragraph [0021] of the specification.

The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted **is** the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

If this issue is not otherwise appropriately remedied, Applicant is required to cancel the new matter in the reply to this Office Action.

Specification

12. The objection to the specification as failing to provide proper antecedent basis for the claimed subject matter, is maintained. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required:

Claim 59 is directed to a process of inducing apoptosis of a natural killer cell comprising contacting the natural killer cell with a polynucleotide encoding SEQ ID NO: 6 or 8 in an amount effective to induce apoptosis of the NK cell.

The specification, as filed, however does not provide antecedent basis for such language.

In the response filed February, 14, 2008, Applicant appears to be arguing that the amendment to paragraph [0021] to insert SEQ ID NOs after the recitation of the GenBank® accession No, provides proper antecedent basis for the claimed methods of inducing apoptosis.

While this amendment might provide proper antecedent basis for claims drawn to polynucleotides encoding such polypeptides, it is submitted that it would not be clear from a reading of the descriptive portion of this application, alone, where there is support for the language of the claims because apart from the listing of the amino acid sequences of SEQ ID NOs: 6 and 8 in the present

Sequence Listing and after their respective GenBank® accession No, there is no other references to these sequences in the disclosure.

In accordance with 37 C.F.R. § 1.78, the claim or claims must conform to the invention as set forth in the remainder of the specification and the terms and phrases used in the claims must find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description.

This is necessary in order to insure certainty in construing the claims in the light of the specification, *Ex parte Kotler,* 1901 C.D. 62, 95 O.G. 2684 (Comm'r Pat. 1901). See 37 C.F.R. § 1.75, M.P.E.P. §§ 608.01(i) and 1302.01.

M.P.E.P. § 608.01(o) states:

> While an applicant is not limited to the nomenclature used in the application as filed, he or she should make appropriate amendment of the specification whenever this nomenclature is departed from by amendment of the claims so as to have clear support or antecedent basis in the specification for the new terms appearing in the claims. This is necessary in order to insure certainty in construing the claims in the light of the specification, *Ex parte Kotler,* 1901 C.D. 62, 95 O.G. 2684 (Comm'r Pat. 1901). See 37 CFR 1.75, MPEP § 608.01(l) and § 1302.01.

M.P.E.P. § 608.01(o) further states that if the examiner determines that the claims presented late in prosecution do not comply with 37 CFR 1.75(d)(1), applicant will be required to make appropriate amendment to the description to provide clear support or antecedent basis for the terms appearing in the claims provided no new matter is introduced.

Accordingly, it is maintained that the disclosure, as filed, does not provide proper antecedent basis for the language of the claimed method. Therefore, Applicant is required to correct this deficiency by appropriately amending the specification ***without*** introducing new matter and in accordance with M.P.E.P. § 608.01(o).

Grounds of Rejection Maintained

Claim Rejections - 35 USC § 112

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. The rejection of claim 59 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a NEW MATTER rejection.

Claim 59 is drawn to a method which recites contacting a natural killer cell with "a polynucleotide encoding SEQ ID NO: 6 or 8".

At pages 13 and 14 of the amendment filed February 14, 2008, Applicant has traversed this ground of rejection and appears to be arguing that the amino acid sequences of SEQ ID NO:6 and 8 have properly been added on August 8, 2007 now that a statement under 37 C.F.R. 1.57 (f) under has been provided.

However, for the reasons set forth above, this statement has been found to be insufficient to properly incorporate the amino acid sequences of SEQ ID NO:6 and 8.

To overcome this NEW MATTER rejection, which specifically pertains to the amino acid sequences of SEQ ID NO:6 and SEQ ID NO:8 being NEW MATTER, it would be remedial to provide a new statement under 37 C.F.R. 1.57 (f) stating that the material which has been inserted **is** the material incorporated by reference and that the previous amendments contain no new matter.

New Grounds of Rejection

Claim Rejections - 35 USC § 101

15. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

16. Claim 59 is rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

The considerations that are made in determining whether a claimed invention is supported by either a specific and substantial asserted utility or a well-established utility are outlined by the published Utility Examination Guidelines (Federal Register; Vol. 66, No. 4, January 5, 2001). A copy of this publication can be viewed or acquired on the Internet at the following address; http://www.gpoaccess.gov.

Briefly, a "specific and substantial" asserted utility is an asserted utility that is specific to the particular nature and substance of the claimed subject matter, and which would be immediately available for application in a "real-world" context by virtue of the existing information disclosed in the specification and/or on the basis of knowledge imparted by the prior art, such that its use would not require or constitute carrying out further research to identify or reasonably confirm its usefulness in this context. A "well-established" utility is a credible, specific, and substantial utility, which is well known, immediately apparent, and implied by the specification, and based on the disclosure of the properties of a material or subject matter, either alone or taken with the knowledge of one skilled in the art.

Claim 59 is drawn to a method of inducing apoptosis of a natural killer (NK) cell comprising contacting the NK cell with a polynucleotide encoding SEQ ID NO: 6 or 8, in an amount effective to induce apoptosis of the NK cell.

In this case, the specification provides no asserted utility for the claimed method other than the asserted utility of inducing apoptosis of a natural killer cell set forth in the method objective. While the specification presents evidence in Figure 6 and at page 32, paragraph [0132] that injection of a mouse IL-21 plasmid into a mouse causes apoptosis, i.e., programmed cell death, of mouse splenic natural killer cells, the specification does not establish that there is a

specific and substantial utility for the asserted utility of inducing apoptosis in a natural killer cell because the specification does not present an immediately available "real-world" use for methods of inducing apoptosis, i.e., programmed cell death, in an NK cell. Notably, the specification instead teaches that *activated* NK cells have an antitumor effect in a mouse model of melanoma (See entire document, e.g., Example 7), and therefore, it is submitted that methods of inducing apoptosis in a NK cell to create *apoptotic* NK cells lack a "specific and substantial" because one of skill in the art could not immediately apply methods of inducing apoptosis in a NK cell in any "real-world" context to immediately benefit the public by virtue of the existing information disclosed in the specification. Similarly, it is submitted that the claimed methods are not supported by any "well-established" utility for inducing apoptosis in a natural kill cell because the art also teaches that it is *activated* NK cells that are known to have an antitumor effect in some mouse tumor models.

For example, Wang et al. (Cancer Research, 63:9016-9022, 2003, of record), teach that "the cytolytic activity of enriched NK cells from mIL-21-treated mice against B16 targets was significantly increased compared with NK cells from pORF-treated mice" (see page 9020, right column), while the antitumor activity of mIL-21 was completely abolished after *in vivo* depletion of NK cells". Similarly, Davis et al (Clin. Cancer Research 13(12): 3630-3636, 2007, IDS filed 2/14/2008) teach that in murine models of metastatic melanoma, renal cell carcinoma, fibrosarcoma, pancreatic carcinoma, colon carcinoma, adenocarcinoma, and thymoma that "[d]epletion studies have shown that the antitumor activity of IL-21 requires CD8+ T cells, NK cells, or both depending on the tumor model" (see page 3631, left column).

Accordingly, it is not apparent the that art recognized any "well-established" utility for inducing apoptosis in a natural killer cell comprising contacting the NK cell with a polynucleotide encoding SEQ ID NO: 6 or 8 in an amount effective to induce apoptosis of the NK cell because contacting an NK cell with a polynucleotide encoding SEQ ID NO: 6 or 8 in an amount effective to

cause its death would create natural killer cells that are not activated, i.e., dead natural killer cells, as opposed to activated natural killer cells.

For these reasons, methods of inducing apoptosis in a natural killer cell comprising contacting the NK cell with a polynucleotide encoding SEQ ID NO: 6 or 8 in an amount effective to induce apoptosis of the NK cell are not supported by either a "specific and substantial" utility or a "well-established" utility. In this case, these methods were not available for use in a "real-world" context, as use of these methods would require carrying out further research to identify if there is a "specific and substantial" utility for inducing apoptosis in a natural killer cell.

In this case, the specification merely presents a wish for methods of inducing apoptosis in a natural killer cell comprising contacting the NK cell with a polynucleotide encoding SEQ ID NO: 6 or 8 in an amount effective to induce apoptosis of the NK cell which are later shown to have a "specific and substantial utility". Therefore, while such methods may indeed have utility *once they are identified*, further research would be required to identify and reasonably confirm their usefulness; so, the claimed invention lacks a "specific and substantial" asserted utility.

To fulfill the requirements of 35 U.S.C. § 101, the skilled artisan must be able to use a claimed invention in the manner asserted by Applicant to provide some immediate benefit to the public. See *Nelson v. Bowler and Crossley*, 206 USPQ 881 (CCPA, 1980).

Furthermore in *Brenner, Comr. Pats. v. Manson*, 148 U.S.P.Q. 689 (US SupCt, 1966), the court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. Id., at 695.

Further, the Court opined,

> [W]e are [not] blind to the prospect that what now seems without "use" may tomorrow command the grateful attention of the public. But a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. Id., at 696.

By analogy, as the instant specification would not permit the skilled artisan to practice the claimed invention of inducing apoptosis in a natural killer cell comprising contacting the NK cell with a polynucleotide encoding SEQ ID NO: 6 or 8 in an amount effective to induce apoptosis of the NK cell, so as to immediately benefit the public, it would not satisfy the utility requirement set forth under 35 U.S.C. § 101. To employ the claimed methods to induce apoptosis in a natural killer cell by contacting the NK cell with a polynucleotide encoding SEQ ID NO: 6 or 8 in an amount effective to induce apoptosis of the NK cell, as its asserted utility, would clearly require further research, which should be regarded as constituting part of the inventive process. Because the specification does not provide a "specific and substantial" asserted utility for the claimed method and because there does not appear to be a "well-established" utility for the claimed method, that would allow one of skill to use the claimed process in a "real world" context so as to immediately benefit the public, the specification merely represents an invitation to the skilled artisan to further elaborate upon the disclosure and complete the inventive process; and for these reasons, the requirements set forth under 35 U.S.C. § 101 have not been met.

Claim Rejections - 35 USC § 112

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claim 59 is also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reasons set forth in above rejection of the claims

under 35 U.S.C. § 101, one skilled in the art clearly would not know how to use the claimed invention.

M.P.E.P. § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

Because the specification does not identify a specific and substantial utility for the claimed invention, it would be necessary to determine if the claimed methods have any specific and substantial utility; therefore, the amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

19. Claim 59 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a NEW MATTER rejection.

Claim 59 which was added after the filing date[2] of the instant application in the amendment filed July, 19, 2005, as currently presented, is drawn to a method of inducing apoptosis of a natural killer (NK) cell comprising contacting the NK cell with a polynucleotide encoding SEQ ID NO: 6 or 8, in an amount effective to induce apoptosis of the NK cell.

In the amendment filed July, 19, 2005, Applicant indicated that support for adding claim 59 can be found in "the specification at, for instance Example 7 and Figure 6". Then in subsequent amendments, Applicant has not indicated where support occurs in the specification for the amendments made to this claim.

MPEP § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims". See M.P.E.P. § 714.02 and § 2163.06. Nevertheless, as M.P.E.P. § 2163 further states: "The examiner has the initial burden of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the original disclosure a description of the invention defined by the claims. See *Wertheim*, 541 F.2d at 263, 191 USPQ at 97".

However, contrary to Applicant's assertion, and upon careful reviewing of the specification, it does not appear that the specification, including the claims, as originally filed, provide adequate support for claim 59, as currently presented.

Notably, Example 7 at page 32, presents the following relevant disclosure pertaining to Figure 6 and methods of inducing apoptosis of a natural killer cell:

> "As shown in Fig. 6a, annexin V staining of NKLI+/CD3" splenic NK cells increased from 16.9% to 41.6% 4 days after mIL-21 plasmid injection, indicating that mIL-21 had an apoptotic effect on NK cells in vivo. … These results demonstrate that IL-21 in vivo can induce NK cell apoptosis …".

Notably, after carefully reviewing the specification, including the claims as

originally filed, the examiner could not find any other disclosure which would reasonably establish a nexus between the far broader subject matter set forth in the instant claims, which, for example, includes methods of inducing apoptosis in any NK cell in any context from any species by contacting the NK cell with either an IL-21 polynucleotide encoding SEQ ID NO:8, which was derived from a mouse or an IL-21 polynucleotide encoding SEQ ID NO:6, which derived from a human and the method of inducing apoptosis set forth in Example 7. Notably, after reviewing the specification, including the claims as originally filed, it is not apparent that the inventors originally contemplated these far broader methods of inducing apoptosis of a natural killer cell, because this disclosure only sets forth a method of inducing apoptosis in murine NK cells *in vivo* by intravenous injection of a plasmid encoding a murine IL-21 polynucleotide into a mouse.

Given the apparent difference in the breadth of the claims and that of the pertinent disclosures, it is submitted that the claim 59 has introduced new concepts, violating the written description requirement set forth under 35 U.S.C. § 112, first paragraph.

Otherwise this issue might be resolved if Applicant were to point to other disclosures in the specification, including the claims, as originally filed, which are believed to provide the necessary written support for the language of the instant claims.

Conclusion

20. No claim is allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935. The Examiner can normally be reached on Monday through Friday 7:00 AM to 4:30 PM with alternate Fridays off.

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[2] The filing date of the instant application is 11/19/04

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Respectfully,
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